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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,494	04/27/2006	Benjamin Oshlack	200.1163US	8290

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EXAMINER	
CLAYTOR, DEIRDRE RENEE	
ART UNIT	PAPER NUMBER
1627	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,494	OSHLACK ET AL.	
	Examiner	Art Unit	
	Renee Claytor	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

Applicants present arguments over the 35 USC 103 rejection over Oshlack et al. (US PgPub 2003/0229111) in view of Kuczynski et al. (US Patent 5,866,164). In particular Applicants argue that it is not obvious to optimize the parameter which was not recognized in the prior art as one that would affect the results. It is argued that the combination of the cited references does not provide a reason to a skilled person to modify the naltrexone to hydrocodone ratio disclosed in the Oshlack publication to the specific ratios recited in the present claims because the cited references do not teach or suggest what a result of such a modification may be. Applicants argue that the Oshlack publication is directed to stabilized naltrexone compositions and the ratios described in Oshlack are much higher than what is presently claimed.

In response to the above arguments, it is noted that Applicants have focused on the examples of Oshlack et al. in making their argument. However, the reference must be taken as a whole when making a rejection. Oshlack does not have to exemplify each and every embodiment of the invention. Oshlack teaches amounts of naltrexone in amounts of greater than 0.001 mg and less than 20 mg and amounts of hydrocodone between 5 and 20 mg. Oshlack teaches that in certain embodiments the composition comprises 5-20 mg of hydrocodone and less than 5 mg of naltrexone. Therefore, if naltrexone is in a dose of 0.056 mg and hydrocodone is 5 mg, then the ratio is 0.011:1. Accordingly, Oshalck et al. does contemplate ranges that would fall in the ratios as presently claimed. Because Oshlack et al. teaches dosage ranges of the compositions

that fall within the ratios claimed, it would be desirable to optimize a dosage range between the two compositions to effectively treat pain. Regarding Applicants arguments that it is not obvious to optimize the parameter which was not recognized in the prior art as one that would affect the results, it is noted that the fact that Applicants have recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would other be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Applicants provide further arguments over the combination of references above. In particular, Applicants argue that the Oshlack publication does not provide a reason for the skill person to formulate a dosage form containing the relative amounts claimed in claims 2-11 and 30-34. Applicants argue over newly added claims 37-38.

In response to the above arguments, it is noted that Oshlack does not teach the exact amounts of naltrexone and hydrocodone, as claimed in claims 2-11 and 30-34, in one composition. However, Oshlack et al. teaches amounts of naltrexone between 0.001-20 mg and of hydrocodone between 5-20 mg, of which the amounts in claims 2-11 and 30-34 fall within those ranges. It would be obvious for one of skill in the art to try different amounts and combinations within those ranges to formulate a composition that will provide maximal pain relief. Applicants have just added new claims 37-38 which will be addressed in the rejection below.

Applicants have not presented arguments over the 35 USC 103 rejeciton over Shermen et al. (US PgPub 2003/0191147) in view of Kaiko et al. (US PgPub 2003/0031712) and Kuczynski et al. (US Patent 5,866,164).

Due to Applicants amendments, please see the modified rejections below.

Claim Rejections -35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-14, 17-19, 22, 27-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oshlack et al. (US Pg-Pub 2003/0229111) in view of Kuczynski et al. (US Patent 5,866,164).

Oshlack et al. teach pharmaceutical compositions comprised of naltrexone in amounts of no greater than 0.01 mg and less than 20 mg (paragraph 0016). Table 20A exemplifies a composition comprising naltrexone hydrochloride in an amount of 0.5 mg and hydrocodone bitartrate in an amount of 5 mg, which falls within the claimed ration of claim 1 (paragraph 0035). Table 20A teaches a composition comprising 0.5 mg of naltrexone and 5 mg of hydrocodone, meeting the limitation of claim 2. Tables 22A, 23A, 24A, 25A, 26A and 27A exemplify a composition comprising naltrexone hydrochloride in an amount of 0.125 mg and hydrocodone bitartrate in amount of 5 mg, which meets the limitation of claims 3-5 (meeting the limitation of "about" 7.5 mg

hydrocodone). It is further taught that the composition has a sustained release coat and this is accomplished with Eudragit RS30D (see Tables 9A, 10A, 11A, 12A, 13A). The examples associated with Tables 20, 22-27 all teach a process of making the compositions of the invention within the claimed ratio.

Oshlack et al. does not teach compositions with the exact amounts of naltrexone and hydrocodone as listed in claims 2-11 and 30-34 in one composition or an osmotic dosage form.

Kuczynski et al. teaches osmotic dosage forms comprising hydrocodone and naltrexone in which hydrocodone and the opioid antagonist (which includes naltrexone) are included together in one layer (see Examples 4 and 7).

It is obvious to vary and/or optimize the amount of hydrocodone and naltrexone provided in the composition, according to the guidance provided by Oshlack et al., to provide a composition having the desired properties such as the desired concentrations of hydrocodone and naltrexone. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). One would be motivated to optimize the amounts of naltrexone and hydrocodone as taught by Oshlack et al. in order to provide maximal pain relief because Oshlack et al. teach ranges of each drug that overlap with the claimed ranges. One would be motivated to formulate the composition in an osmotic dosage form according to the teachings of Kuczynski et al. to ensure delivery of a therapeutically

effective dose at a controlled rate over a sustained period of time and to prevent opioid abuse (Col. 8, lines 20-35).

Claims 1-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherman et al. (US Pg-Pub 2003/0191147) in view of Kaiko et al. (US PgPub 2003/0031712) and Kuczynski et al. (US Patent 5,866,164).

Sherman et al. teach compositions comprised of naltrexone hydrochloride in amounts of about 0.1 to less than about 0.5 mg (paragraphs 0058 and 0065). Paragraphs 0062-0063 exemplify the dose amounts of naltrexone contemplated by the invention and conclude to say that any minimum amount and any maximum amount within range of amounts is possible (paragraph 0064). The composition is taught as also having another ingredient in the way of an opioid agonist such as hydrocodone bitartrate (paragraph 0068 and Example 15). Example 15 exemplifies the two compounds in a composition that falls within the claimed ratio. Paragraphs 0242-0251 exemplify a study in which the composition of the invention was tested in methods of treating pain. Further controlled release compositions are also contemplated by Sherman et al. (paragraph 0145). Sherman et al. further teaches that in preparing a composition, amounts of naltrexone at 0.1 % and hydrocodone at 10% are added into a mixture before granulation in Example 15, meeting the limitation of the claimed ratio. Sherman further teaches that other active pharmaceutical ingredients such as ibuprofen (paragraph 0069). Sherman teaches oral dosage forms of the compositions

(paragraphs 0070-0071). Sherman teaches the state of the art regarding opioid antagonists being manufactured to prevent abuse of opioid agonists (paragraph 0056).

Sherman et al. does not teach the exact amounts of naltrexone and hydrocodone as listed in claims 2-11 in one composition or that the compositions are interdispersed with a sustained release excipient or an osmotic dosage form.

Kaiko et al. teaches formulations comprising hydrocodone and naltrexone (paragraph 0072) can comprise coatings and melt extrusion multiparticulates that aid in releasing the drug over a twelve to twenty-four hour period to provide analgesia (paragraph 0099). Kaiko discusses that opioid antagonists typically block or reverse all of the effects of opioid agonists and that a use of opioid antagonists is as a once-a-day treatment of naltrexone to block the euphoric affects that might otherwise be obtained upon administration of opioids to addicts (paragraph 0011). Kaiko teaches incorporating the opioid agonist and the opioid antagonist into a dosage form that includes a sustained release carrier such that the oral dosage form can be administered on a twice-a-day or once-a-day basis (paragraph 0046).

Kuczynski et al. teaches osmotic dosage forms comprising hydrocodone and naltrexone in which hydrocodone and the opioid antagonist (which includes naltrexone) are included together in one layer (see Examples 4 and 7).

Furthermore, it is obvious to vary and/or optimize the amount of naltrexone and hydrocodone provided in the composition, according to the guidance provided by Sherman et al., to provide a composition having the desired properties such as the desired concentrations of both drugs in an effort to provide maximal pain relief. It is

noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Accordingly, one of ordinary skill in the art at the time of the invention would have found it obvious to combine the teachings of Sherman et al. which teaches pharmaceutical compositions and methods of making and using such compositions that are comprised of hydrocodone and naltrexone with the teachings of Kaiko et al. which teach similar compositions in which the drugs are interdispersed with sustained release excipients and Kuczynski et al. which teaches osmotic dosage forms comprised of hydrocodone and naltrexone in one layer. One would be motivated to do so in an effort to treat pain over a maximal period of time, to increase patient compliance and to reduce the abuse potential of the opioid agonist.

Conclusion

Claim 38 is objected to for being dependent on rejected claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is (571)272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

/SREENI PADMANABHAN/
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